The opinion in support of the decision being entered today was *not* written for publication and is *not* binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte MANFRED ASSMUS and HANS-ULRICH PETEREIT

Appeal No. 2004-1618
Application 08/813,950

HEARD: NOVEMBER 17, 2004

Before OWENS, TIMM and JEFFREY T. SMITH, *Administrative Patent Judges.*

OWENS, *Administrative Patent Judge.*

DECISION ON APPEAL

This appeal is from a rejection of claims 25-29. Claims 1, 3, 5, 7, 9, 11, 13 and 15, which are all of the other pending claims, stand withdrawn from consideration by the examiner as being directed toward a nonelected invention.

THE INVENTION

The appellants claim an oral or dermal medicinal composition having a thermoplastic coating and binding agent consisting essentially of a thermoplastic acrylic plastic and 20-50 wt% of glycerol monostearate. Claim 25 is illustrative:

> 25. An oral or dermal medicinal composition containing a pharmaceutical active substance and a thermoplastic coating and binding agent prepared by a method of applying a thermoplastic coating and binding agent in a hot-melt liquid state at a temperature of 100-150°C to said oral or dermal medicinal composition, followed by cooling to solidify the thermoplastic coating and binding agent, wherein said thermoplastic coating and binding agent consists essentially of a mixture of, based on 100% by weight of A and B:
>
> A) a thermoplastic acrylic plastic with a melting temperature above room temperature and below 200°C, a glass transition temperature below 120°C, and a melt viscosity of 1,000 to 1,000,000 Pa-sec at the melting temperature; and
>
> B) 20-50 wt.% of glycerol monostearate, wherein the glass transition temperature of the mixture is no more than 20°K below the glass transition temperature of component A.

THE REFERENCES

Rudnic et al. (Rudnic)	5,484,608	Jan. 16, 1996
Mueller et al. (Mueller)	5,552,159	Sep. 3, 1996
Burguiere et al. (Burguiere)	5,603,957	Feb. 18, 1997 (filed Apr. 13, 1994)
Pöllinger et al. (Pöllinger)	5,695,784	Dec. 9, 1997 (effective filing date Jan. 6, 1993)
Yajima et al. (Yajima)	5,707,646	Jan. 13, 1998 (§ 102(e) date Sep. 9, 1994)

Staniforth et al. (Staniforth) 5,858,412 Jan. 12, 1999
(effective filing date on or before Jul. 8, 1996)[1]

Arai (JP '317)[2] 51-091317 Aug. 10, 1976
(Japanese kokai)

K. Lehmann et al. (Petereit)[3], "Fast Disintegrating Controlled Release Tablets from Coated Particles", 37 *Drugs Made in Germany* 53-60[4] (ECV 1994).

THE REJECTIONS

The claims stand rejected under 35 U.S.C. § 103 as follows: claims 25-29 over Petereit; claims 25-29 over Yajima; claims 25-29 over Burguiere in view of Mueller; claims 25-28 over Staniforth in view of Mueller; claims 25-29 over JP '317, Rudnic and Pöllinger in view of Petereit and Mueller; and claims 25-28 over Mueller in view of Burguiere and Petereit.

OPINION

We affirm the rejections over 1) Petereit, 2) Burguiere in view of Mueller, 3) JP '317, Rudnic and Pöllinger in view of Petereit and Mueller, and 4) Mueller in view of Burguiere and

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[1] There is no dispute as to whether Staniforth is prior art.

[2] Our consideration of JP '317 is based upon the English translation thereof which is of record.

[3] The examiner and the appellants refer to this reference as "Petereit". For consistency, we likewise do so.

[4] We refer to the pages as numbered in the article, i.e., 1 to 8.

Petereit. We reverse the rejections over 1) Yajima and 2) Staniforth in view of Mueller.

The appellants state that claim 29 stands or falls separately from claim 25 (brief, page 3). Claims 26-28 therefore stand or fall with claim 25 which is the sole independent claim. *See In re Ochiai*, 71 F.3d 1565, 1566 n.2, 37 USPQ2d 1127, 1129 n.2 (Fed. Cir. 1995); 37 CFR § 1.192(c)(7)(1997).

Rejection over Petereit

Petereit discloses oral medicinal compositions containing drug particles such as crystals, granules and pellets coated with aqueous dispersions of methacrylic acid and methacrylic ester copolymers and compressed into fast disintegrating tablets (page 1). The copolymers include Eudragit® RL and RS (pages 1 and 2) which are among the appellants' copolymers (specification, page 11, line 8). Tableting excipients are useful in an amount of 25-50% to reduce the stress to the coatings during the tableting process, fill the interspace, and give the desired fast disintegration of the tablets (page 8). The disclosed excipients include glyceryl monostearate (page 2).

The appellants argue that in Petereit's table 1, glycerol monostearate is used in an amount of only 3.0 to 8.8% of the combined Eudragit® and glycerol monostearate (brief, pages 6 and 7). This argument is not well taken because Petereit's disclosure is not limited to the examples. *See In re Fracalossi*, 681 F.2d 792, 794 n.1, 215 USPQ 569, 570 n.1 (CCPA 1982); *In re Mills*, 470 F.2d 649, 651, 176 USPQ 196, 198 (CCPA 1972). Instead, all of Petereit's disclosure must be evaluated for what it would have fairly suggested to one of ordinary skill in the art. *See In re Boe*, 355 F.2d 961, 965, 148 USPQ 507, 510 (CCPA 1966). Petereit's disclosure of using 25-50% excipients would have fairly suggested, to one of ordinary skill in the art, use of 25-50% of any of the excipients, alone or in any combination.

The appellants point out that Petereit discloses spray coating formulations rather than hot melt preparations (brief, page 6). When the appellants' product made by a recited process and the product of the prior art appear to be identical or substantially identical, the burden shifts to the appellants to provide evidence that the prior art product does not necessarily or inherently possess the relied-upon characteristics of the appellants' claimed product. *See In re Fitzgerald*, 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980); *In re Best*, 562 F.2d 1252,

1255, 195 USPQ 430, 433-34 (CCPA 1977). The examiner argues that because Petereit's Eudragit® and glycerol monostearate are components used by the appellants and can be used in the appellants' amounts, Petereit's product made from those components appears to be the same or substantially the same as the appellants' product (answer, page 5). Because this argument has not been challenged by the appellants, we accept it as being correct.

We therefore conclude that the compositions claimed in the appellants' claim 25, as well as claim 29 which requires 33.3 to 50 wt% glycerol monostearate, would have been *prima facie* obvious to one of ordinary skill in the art over Petering.

The appellants argue that the first and supplemental Assmus declarations (filed, respectively, June 21, 1999 and October 5, 1999) show unexpected results (brief, pages 4-5; reply brief, pages 2-3). For the following reasons, the evidence in the declarations is not sufficient for overcoming the *prima facie* case of obviousness.

The first declaration does not provide a comparison of the claimed invention with the closest prior art. *See In re Baxter Travenol Labs.*, 952 F.2d 388, 392, 21 USPQ2d 1281, 1285 (Fed. Cir. 1991); *In re De Blauwe*, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984). The first declaration merely provides results at 60°C, 65°C and 80°C, all of which are outside the temperature range recited in the appellants' claims. The appellants argue that "there has never been an issue regarding the effectiveness of the present invention at the recited temperature range of 100-150°C. The purpose of the first Assmus Declaration was to demonstrate ineffectiveness at lower temperatures" (reply brief, page 2). To show unexpected results of the claimed invention relative to the prior art, the evidence necessarily must compare the claimed invention with the prior art, and the first declaration does not do so.

The supplemental declaration does not present evidence which is effective for showing unexpected results. *See In re Freeman*, 474 F.2d 1318, 1324, 177 USPQ 139, 143 (CCPA 1973); *In re Klosak*, 455 F.2d 1077, 1080, 173 USPQ 14, 16 (CCPA 1972). The conclusion in the supplemental declaration is that none of the melts at 65°C was homogeneous (page 2). The photographs and the results in the table, however, merely show that the polymer particles are

smoother when the melt temperature is 150°C. The appellants have not established that polymer particle smoothness correlates with melt homogeneity. Moreover, when the flow improver is glycerol monostearate, the polymer particles obtained using a melt temperature of 100°C are as similar to the particles obtained using a melt temperature of 65°C as they are to the particles obtained using a melt temperature of 150°C.

Second, the evidence presented in the supplemental declaration is not commensurate in scope with the appellants' claims 25 and 29. *See In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 778 (Fed. Cir. 1983); *In re Clemens*, 622 F.2d 1029, 1035, 206 USPQ 289, 296 (CCPA 1980). The appellants' claims 25 and 29 encompass a great variety of thermoplastic acrylic plastics and relative amounts of thermoplastic acrylic plastic and glycerol monostearate, yet only one thermoplastic acrylic polymer and one amount (50%) of glycerol monostearate within the appellants' recited range were used. We find in the evidence of record no reasonable basis for concluding that the great number of materials encompassed by the appellants' claims would behave as a class in the same manner as the particular materials tested.

See In re Lindner, 457 F.2d 506, 508, 173 USPQ 356, 358 (CCPA 1972); *In re Susi*, 440 F.2d 442, 445-46, 169 USPQ 423, 426 (CCPA 1971).

For the above reasons we conclude that the composition claimed in the appellants' claims 25 and 29 would have been obvious to one of ordinary skill in the art over Petereit.

Rejection over Yajima

Yajima discloses an oral medicinal composition containing 1) a complex formed by dispersing or dissolving an unpleasantly tasting basic drug and a functional polymer compound in a substance having a low melting point, 2) 10 to 70 wt%, based on the composition, of sugar alcohol, and 3) 0.1 to 7 wt%, based on the composition, of basic oxide (col. 2, lines 45-51). The functional polymer can be Eudragit® E (col. 2, lines 59-60), which is one of the appellants' thermoplastic acrylic plastics (specification, page 11, line 8), and can be 1 to 60 wt% of the complex (col. 3, lines 7-8). The preferred substances having a low melting point include glycerin monostearate (col. 3, line 5). Yajima teaches that "without any organic solvent, a functional polymer can be dissolved or dispersed in a substance having a low melting point when the substance having a low melting point has been melted" (col. 2, lines 9-12). In examples 4, 7 and 13,

100 g of Eudragit® E are dispersed in 600 g of glyceryl monostearate which has been melted at 100°C, and 300 g of a drug are dispersed in the mixture.

The examiner argues that Yajima's "amount of glycerol monostearate ranges from the minimum amount required to dissolve or disperse the functional polymer (col. 2, lines 9-12) to 98% by weight (100% by weight of all components in the complex - 1% drug - 1% of functional polymer = 98% by weight)" (answer, page 6). The examiner further argues (answer, page 22):

> Examples 4, 7 and 13 show a ratio of glycerol monostearate to Eudragit E polymer of 6:1 for a complex containing 10% by weight of polymer. A complex containing the minimum 1% by weight of polymer would necessitate only 6% by weight of glycerol monostearate based on the 6:1 ratio exhibited predominantly throughout the examples of the patent.
> 56. Accordingly, a glycerol monostearate content of from 6% by weight up to 98% by weight of glycerol monostearate is within the ambit of Yajima et al. which encompasses the claimed range of from 20-50 wt.%.

The appellants' claim 25, however, requires that the amount of glycerol monostearate is 20-50 wt% of the thermoplastic acrylic plastic plus glycerol monostearate, not 20-50 wt% of the complex. Thus, if the amount of thermoplastic acrylic plastic is 1 wt% as proposed by the examiner, the glycerol monostearate must be 0.25 to 1.0 wt%. The examiner has not established that Yajima's examples 4, 7 and 13, wherein the amount of glycerol

monostearate is 6 times the amount of Eudragit® E, or any other disclosure by Yajima, would have fairly suggested, to one of ordinary skill in the art, an amount of glycerol monostearate that is 20-50 wt% of the combined amounts of Eudragit® E and glycerol monostearate.

Accordingly, we reverse the rejection over Yajima.

Rejections over Burguiere in view of Mueller, and over Mueller in view of Burguiere and Petereit

Mueller discloses a solid depot drug form which can be tablets, coated tablet cores, pellets, granules or suppositories, and is made by melt extrusion at 50 to 200°C (col. 1, line 62 - col. 2, line 16). The drug form includes at least 6% of at least one water-insoluble poly(meth)acrylate having a glass transition temperature of -60 to 180°C, the disclosed poly(meth)acrylates including Eudragit® RS and Eudragit® RL (col. 4, lines 15 and 45-46), which are among the appellant's thermoplastic acrylic plastics (specification, page 11, line 8). The drug form can include up to 30 wt% of one or more conventional pharmaceutical auxiliaries (col. 2, lines 11-12), the disclosed auxiliaries including plasticizers (col. 3, line 6).

Mueller does not disclose glycerol monostearate as a plasticizer. However, the teaching by Burguiere that in a solid drug form including Eudragit® RL and/or RS as a film-forming polymer (col. 6, line 11), suitable plasticizers include stearates of a glycol such as glycerol (col. 6, lines 35-36) would have fairly suggested, to one of ordinary skill in the art, the use of glycerol monostearate as the plasticizer in Mueller's solid drug form. Hence, we are not persuaded by the appellants' argument that Burguiere does not specifically disclose the monostearate of glycerol (brief, page 11).

The appellants argue that "[w]hile Mueller et al discloses a solid depot drug form produced by melt extrusion at from 50° to 200°C, Mueller et al discloses and suggests nothing with regard to the presently-recited requirement of a hot-melt liquid state at a temperature of 100-150°C" (brief, page 10). This argument is not persuasive because the disclosure of a temperature range of 50-200°C would have fairly suggested, to one of ordinary skill in the art, any temperature within that range, including temperatures of 100-150°C.

The appellants argue that "Mueller et al do not require plasticizers and thus, there would be no reason for one skilled in the art to add such a plasticizer for the melt extrusion-processed solid depot drug of Mueller et al, let alone in an amount as high as 20% based on the water-insoluble poly(meth)acrylate component of Mueller et al" (brief, page 16). Mueller teaches that the finished depot form can contain 0-30 wt% of one or more conventional pharmaceutical auxiliaries, and that those auxiliaries include plasticizers (col. 2, lines 11-12; col. 2, line 66 - col. 3, line 6). Hence, Mueller would have fairly suggested, to one of ordinary skill in the art, including in the finished depot form up to 30 wt% of a plasticizer. As for the argument that Mueller would not have suggested an amount of plasticizer that is as high as 20 wt% based on the water-insoluble poly(meth)acrylate component, Mueller's disclosed amount of water-insoluble poly(meth)acrylate component is at least 6 wt% of the complete depot form. For an amount of water-insoluble poly(meth)acrylate component of 6 wt%, the amount of plasticizer needed for the plasticizer to be 20-50 wt% of the combined water-insoluble poly(meth)acrylate component and plasticizer is 0.15-6 wt%, which is within Mueller's 0-30 wt% range. Thus, Mueller and Burguiere would have fairly suggested,

to one of ordinary skill in the art, the amounts of glycerol monostearate recited in the appellants' claims 25 and 29.

The appellants argue that without the appellants' disclosure, one of ordinary skill in the art would not have been led to select Mueller's plasticizer such that the glass transition temperature of the combined water-insoluble poly(meth)acrylate component and plasticizer is no more than 20°K below the glass transition temperature of the water-insoluble poly(meth)acrylate component (brief, page 16). As discussed above, Mueller and Burguiere would have fairly suggested, to one of ordinary skill in the art, the use of Eudragit® RS or RL in combination with glycerol monostearate in the relative amounts used by the appellants. Because this combination is the same as that used by the appellants, it necessarily would have the same glass transition temperature relative to that of the Eudragit® RS or RL.

Additionally, the appellants' claimed composition would have been fairly suggested to one of ordinary skill in the art by Petereit for the reasons given above regarding the rejection over that reference applied alone.

The appellants argue that the first and supplemental Assmus declarations show unexpected results over the combined teachings of Mueller and Burguiere (brief, page 10). This argument is not persuasive for the reasons given above regarding the rejection over Petereit applied alone.

Rejection over Staniforth in view of Mueller

Staniforth discloses sustained release solid dosage forms such as tablets or capsules which contain an active ingredient, microcrystalline cellulose, a surfactant as a compressibility augmenting agent, and a sustained release carrier (col. 1, lines 15-16; col. 5, lines 5-9; col. 10, lines 32-33). The disclosed surfactants include glycerol monostearate (col. 11, lines 31-33). The dosage form can be coated with a sustained release coating that can be Eudragit® RS or RL (col. 19, line 66 - col. 20, line 6; col. 20, line 30). The sustained release coating "may be applied in any pharmaceutically acceptable manner known to those skilled in the art" (col. 21, lines 27-29).

The examiner argues that Staniforth's dosage form contains "as much as about 20% by weight (col. 13, lines 37-40) of a surfactant such as glycerol monostearate (col. 11, line 33)" (answer, page 9). What Staniforth discloses is that "the surfactant is added to the suspension or slurry in amounts

ranging from about 0.1% to about 20% by weight, preferably from about 0.1 to about 5% by weight, based on the amount of microcrystalline cellulose" (col. 13, lines 37-40). Thus, the disclosed amount of surfactant is based upon the microcrystalline cellulose rather than the sustained release coating plus surfactant.

The examiner has not explained how Staniforth would have fairly suggested, to one of ordinary skill in the art, an amount of surfactant that is 20-50 wt% of the combined amount of sustained release coating and surfactant. Hence, the examiner has not established a *prima facie* case of obviousness of the appellants' claimed invention over the combined teachings of Staniforth and Muller. We therefore reverse the rejection over Staniforth in view of Muller.

Rejection over JP '317, Rudnic and Pöllinger in view of Petereit and Mueller

Pöllinger discloses an oral medicinal composition comprising microgranules coated in customary coater equipment with a mixture of water-insoluble and water-soluble components which preferably are, respectively, Eudragit® NE 30 D and hydroxypropylmethyl-cellulose in a ratio of 100:20 to 100:50 (col. 1, lines 6-7; col. 4, lines 26-30 and 60-61; col. 5, lines 25-29). Eudragit®

RL 30 D is disclosed as an alternative to Eudragit® NE 30 D as a film forming agent (col. 5, lines 2-6). The coating can contain glycerol monostearate in an amount of 0.001-20% as a wetting agent (col. 5, line 64 - col. 6, line 14), and can contain glycerol monostearate as a plasticizer (col. 5, lines 49-53).

Mueller does not disclose glycerol monostearate as a plasticizer. However, the teaching by Pöllinger that in a solid drug form including Eudragit® NE 30 D or RL 30 D as a film-forming polymer (col. 5, lines 2-6), the suitable plasticizers include glycerol monostearate (col. 5, lines 49-53) would have fairly suggested, to one of ordinary skill in the art, the use of glycerol monostearate as the plasticizer in Mueller's solid drug form.

Mueller discloses the following advantages of melt extrusion over granulation and tableting (col. 1, lines 36-46):

> The advantage of extrusion over other techniques such as granulation and tabletting [sic] is that the technology is simple, solvents are avoided, the number and amount of auxiliaries is minimized, it is possible to prepare fixed solutions, elaborate mixing processes are avoided and, in particular, the possibility of demixing of the components is avoided, in other words the composition of the individual depot forms throughout production is reliably absolutely constant. In addition there are the advantages of a continuous process with high throughput and small material losses.

It would have been *prima facie* obvious to one of ordinary skill in the art to use melt extrusion to make Pöllinger's microgranules to obtain the benefits disclosed by Mueller of melt extrusion over other customary coating techniques.

Moreover, the appellants' claimed composition would have been fairly suggested to one of ordinary skill in the art by Petereit for the reasons given above regarding the rejection over that reference applied alone.

The appellant argues that "[w]hile Pöllinger et al lists various film-forming agents known in the art (column 4, line 45 ff), only some Eudragit brand, but not all Eudragit brand, polymers may be used in Pöllinger et al (column 4, line 66 ff). For example, Eudragit brand polymers that are cationic did not produce the desired results (column 5, line 44 [sic, 34] ff)" (brief, page 14). That argument is not convincing because Pöllinger's disclosure that film formers such as Eudragit® RL 30 D and NE 30 D (col. 5, lines 2-4) are effective would have led one of ordinary skill in the art to use them.

The appellants argue that "[n]one of the examples in Pöllinger et al contain GMS [glycerol monostearate] and thus, no percentage range therefore is disclosed" (brief, page 14). We are not persuaded by this argument because Pöllinger is not limited to its examples. *See Fracalossi*, 681 F.2d at 794 n.1, 215 USPQ at 570 n.1; *Mills*, 470 F.2d at 651, 176 USPQ at 198. Pöllinger's disclosure of 0.001-20% of wetting agent, which can be glycerol monostearate (col. 6, lines 3 and 15), would have fairly suggested any amount of glycerol monostearate within that range to one of ordinary skill in the art.

The appellants argue that without their disclosure as a guide, one of ordinary skill in the art would not have arrived at a glass transition temperature of a mixture of thermoplastic acrylic plastic and glycerol monostearate that is no more than 20°K below the glass transition temperature of the thermoplastic acrylic plastic (brief, page 14). Because Pöllinger's Eudragit® RL 30 D and glycerol monostearate are the same materials used by the appellants, their mixture in the amounts used by the appellants necessarily would have the glass transition temperature of the appellants' mixture.

The appellants argue that JP '317, Rudnic, Pöllinger, Petereit and Mueller do not disclose or suggest a composition having an amount of glycerol monostearate as high as 33.3 wt% as required by the appellants' claim 29 (brief, page 15). Pöllinger discloses that Eudragit® NE 30 D can be used in combination with hydroxyropylmethylcellulose in ratios of 100:20 to 100:50, and that the wetting agent, which can be glycerol monostearate, can be present in an amount of 0.001-20% (col. 5, lines 25-29; col. 6, lines 3 and 15). Pöllinger, therefore, would have fairly suggested, to one of ordinary skill in the art, amounts of glycerol monostearate which, based on the combination of Eudragit® NE 30 D and glycerol monostearate, are higher than 20%, e.g., 33.3%.

The appellants argue that the first and supplemental Assmus declarations show unexpected results over the combined teachings of JP '317, Rudnic, Pöllinger, Petereit and Mueller (brief, page 14). This argument is not persuasive for the reasons given above regarding the rejection over Petereit applied alone.

We therefore conclude that the compositions claimed in the appellants' claims 25 and 29 would have been obvious to one of ordinary skill in the art over the combined teachings of JP '317, Rudnic, Pöllinger, Petereit and Mueller.[5]

DECISION

The rejections under 35 U.S.C. § 103 of claims 25-29 over Petereit, claims 25-29 over Burguiere in view of Mueller, claims 25-29 over JP '317, Rudnic and Pöllinger in view of Petereit and Mueller, and claims 25-28 over Mueller in view of Burguiere and Petereit, are affirmed. The rejections under 35 U.S.C. § 103 of claims 25-29 over Yajima and claims 25-28 over Staniforth in view of Mueller are reversed.

[5] A discussion of JP '317 and Rudnic is not necessary to our decision.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

TERRY J. OWENS Administrative Patent Judge	)
CATHERINE TIMM Administrative Patent Judge	) BOARD OF PATENT) APPEALS AND
JEFFREY T. SMITH Administrative Patent Judge	) INTERFERENCES

TJO/ki

Appeal No. 2004-1618
Application 08/813,950

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